

DT02 Rec'd PCT/PT 0 4 FEB 2005

PCT

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

|                  |  |                 |                  |
|------------------|--|-----------------|------------------|
| Applicant(s)     | David Brown, et al.  | Examiner:       | Unassigned       |
| Serial No.:      | 10/519,534   | Group Art Unit: | Unassigned       |
| Confirmation No: | Unassigned   | Docket:         | 178-312 PCT/US   |
| Filed:           | December 27, 2004  | Dated:          | February 2, 2005 |
| For:             | METHOD FOR REDUCING<br>C-REACTIVE PROTEIN<br>LEVELS WITH NON-<br>ANTIBACTERIAL<br>TETRACYCLINE<br>FORMULATIONS |                 |                  |

Commissioner for Patents  
PO Box 1450  
Alexandria, Virginia 22313-01450

*I hereby certify this correspondence is being deposited  
with the United States Postal Service as first class mail,  
postpaid in an envelope, addressed to:  
Commissioner for Patents, PO Box 1450, Alexandria,  
Virginia, 22313-1450  
on February 2, 2005*

Dated: 2/2/05

*Deanna Baye*

INFORMATION DISCLOSURE STATEMENT

Sir:

In order to fulfill the requirements of candor and good faith set forth in 37 C.F.R. §1.56, Applicants submit herewith the following Information Disclosure Statement in accordance with the provisions of 37 C.F.R. §1.97 and §1.98.

UNITED STATES PATENTS

| <u>PATENTEE</u> | <u>PATENT NO.</u> | <u>ISSUE DATE</u> |
|-----------------|-------------------|-------------------|
| Thompson et al. | 5,834,449         | November 10, 1998 |

### **NON-PATENT PUBLICATIONS**

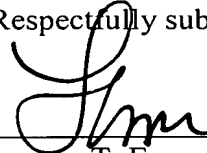
1. Taubes, Gary, "Does Inflammation Cut to the Heart of the Matter?," *Science* (2002) 296: 11-14.
2. Gurfinkel, E., et al. "Treatment with the Antibiotic Roxithromycin in Patients with Acute non-Q-wave Coronary Syndromes. The Final Report of ROXIS study," *European Heart Journal* (1999) 20(2): 121-127.
3. Mosorin M., et al. "Use of Doxycycline to Decrease the Growth Rate of Abdominal Aortic Aneurysms: a Randomized, Double-Blind, Placebo-Controlled Pilot Study," *Journal of Vascular Surgery* (2001) 34(4): 757-758.
4. Gupta, Sandeep, et al., "Elevated *Chlamydia pneumoniae* Antibodies, Cardiovascular Events, and Azithromycin in Male Survivors of Myocardial Infarction," *Circulation* (1997) 96: 404-407.
5. Lusis, Aldons J., "Atherosclerosis," *Nature* (2000) 407:233-241.
6. Meler CR, et al., "Antibiotic Use and Risk of Myocardial Infarction," *JAMA* (1999) 282(21): 1997-1998.
7. Takeshita, Satoshi, et al. "Modulation of Oxidative Burst of Neutrophils by Doxycycline in Patients with Acute Myocardial Infarction," *Journal of Antimicrobial Chemotherapy* (2002) 49: 411-413.
8. Creemers, Esther E.J.M., et al., "Matrix Metalloproteinase Inhibition After Myocardial Infarction," *Circulation Research* (2001) 89: 201-210.
9. Meier, Christoph R., et al., "Antibiotics and Risk of Subsequent First-time Acute Myocardial Infarction," *JAMA* (1999) 281(5): 427-431.
10. Ridker, Paul M., et al., "Long-Term Effects of Pravastatin on Plasma Concentration of C-reactive Protein," *Circulation* (1999) 100: 230-235.
11. Brown, David L., et al., "Clinical and Biochemical Results of the Metalloproteinase Inhibition With Low-dose Doxycycline to Prevent Acute Coronary Syndromes (Midas) Pilot Trial," *American Heart Association* (2001)
12. Libby, Peter, "Atherosclerosis: The New View," *Scientific American* (2002) 48-55.
13. Kloppenburg, M., et al., "Minocycline in Active Rheumatoid Arthritis," *Annals of the New York Academy of Sciences* (1994) 732: 422-423.

Application No.: 10/51 [REDACTED]  
Filing Date: December 27, 2004  
Docket No.: 178-312 PCT/US  
Page 3 of 3

The above-referenced documents are listed on PTO Form 1449. We have enclosed the cited document to facilitate reference to it.

Applicants are not aware of any other references to be identified at this time. If the Examiner has any questions or comments relating to the present application, he or she is respectfully invited to contact Applicants' attorney at the telephone number set forth below.

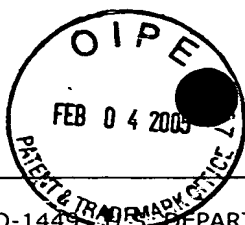
Respectfully submitted,



---

Lauren T. Emr  
Registration No.: 46,139  
Attorney for Applicant(s)

HOFFMANN & BARON, LLP  
6900 Jericho Turnpike  
Syosset, New York 11791  
(516) 822-3550  
LTE/dlb



|   |                                    |                                |
|---|------------------------------------|--------------------------------|
| FORM PTO-1449<br>(Rev. 2-32) PATENT AND TRADEMARK OFFICE<br><br>INFORMATION DISCLOSURE<br>STATEMENT BY APPLICANT<br><br>(Use several sheets if necessary) | ATTY. DOCKET NO.<br>178-312 PCT/US | SERIAL NO.<br>10/519,534       |
|   | APPLICANT<br>Brown et al.          | CONFIRMATION NO.<br>Unassigned |
|   | FILING DATE<br>December 27, 2004   | GROUP<br>Unassigned            |

## U.S. PATENT PUBLICATIONS

| EXAMINER<br>INITIAL |  | DOCUMENT<br>NUMBER | DATE | NAME | CLASS | SUB<br>CLASS | FILING DATE<br>IF APPROPRIATE |
|---------------------|--|--------------------|------|------|-------|--------------|-------------------------------|
|                     |  |                    |      |      |       |              |                               |

## U.S. PATENT DOCUMENTS

| EXAMINER<br>INITIAL |  | DOCUMENT<br>NUMBER | DATE       | NAME            | CLASS | SUB<br>CLASS | FILING DATE<br>IF APPROPRIATE |
|---------------------|--|--------------------|------------|-----------------|-------|--------------|-------------------------------|
|                     |  | 5,834,449          | 11/10/1998 | Thompson et al. |       |              |                               |

## FOREIGN PATENT DOCUMENTS

| EXAMINER<br>INITIAL |  | DOCUMENT<br>NUMBER | DATE | COUNTRY | CLASS | SUB<br>CLASS | TRANSLATION |    |
|---------------------|--|--------------------|------|---------|-------|--------------|-------------|----|
|                     |  |                    |      |         |       |              | YES         | NO |
|                     |  |                    |      |         |       |              |             |    |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|  |  |  |   |
|--|--|--|---|
|  |  |  | Taubes, Gary, "Does Inflammation Cut to the Heart of the Matter?," <i>Science</i> (2002) 296: 11-14.  |
|  |  |  | Gurfinkel, E., et al. "Treatment with the Antibiotic Roxithromycin in Patients with Acute non-Q-wave Coronary Syndromes. The Final Report of ROXIS study," <i>European Heart Journal</i> (1999) 20(2): 121-127.           |
|  |  |  | Mosorin M., et al. "Use of Doxycycline to Decrease the Growth Rate of Abdonminal Aortic Aneurysms: a Randomized, Double-Blind, Placebo-Controlled Pilot Study," <i>Journal of Vascular Surgery</i> (2001) 34(4): 757-758. |

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication with applicant.

|   |                                    |                                |
|---|------------------------------------|--------------------------------|
| FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE<br>(Rev. 2-32) PATENT AND TRADEMARK OFFICE<br><br>INFORMATION DISCLOSURE<br>STATEMENT BY APPLICANT<br><br>(Use several sheets if necessary) | ATTY. DOCKET NO.<br>178-312 PCT/US | SERIAL NO.<br>10/519,534       |
|   | APPLICANT<br>Brown et al.          | CONFIRMATION NO.<br>Unassigned |
|   | FILING DATE<br>December 27, 2004   | GROUP<br>Unassigned            |

## U.S. PATENT PUBLICATIONS

| EXAMINER<br>INITIAL |  | DOCUMENT<br>NUMBER | DATE | NAME | CLASS | SUB<br>CLASS | FILING DATE<br>IF APPROPRIATE |
|---------------------|--|--------------------|------|------|-------|--------------|-------------------------------|
|                     |  |                    |      |      |       |              |                               |

## U.S. PATENT DOCUMENTS

| EXAMINER<br>INITIAL |  | DOCUMENT<br>NUMBER | DATE | NAME | CLASS | SUB<br>CLASS | FILING DATE<br>IF APPROPRIATE |
|---------------------|--|--------------------|------|------|-------|--------------|-------------------------------|
|                     |  |                    |      |      |       |              |                               |

## FOREIGN PATENT DOCUMENTS

| EXAMINER<br>INITIAL |  | DOCUMENT<br>NUMBER | DATE | COUNTRY | CLASS | SUB<br>CLASS | TRANSLATION |    |
|---------------------|--|--------------------|------|---------|-------|--------------|-------------|----|
|                     |  |                    |      |         |       |              | YES         | NO |
|                     |  |                    |      |         |       |              |             |    |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|  |  |  |   |
|--|--|--|---|
|  |  |  | Gupta, Sandeep, et al., "Elevated <i>Chlamydia pneumoniae</i> Antibodies, Cardiovascular Events, and Azithromycin in Male Survivors of Myocardial Infarction," <i>Circulation</i> (1997) 96: 404-407. |
|  |  |  | Lusis, Aldons J., "Atherosclerosis," <i>Nature</i> (2000) 407:233-241.  |
|  |  |  | Meler CR, et al., "Antibiotic Use and Risk of Myocardial Infarction," <i>JAMA</i> (1999) 282(21): 1997-1998.  |

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication with applicant.

|   |                                    |                                |
|---|------------------------------------|--------------------------------|
| FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE<br>(Rev. 2-32) PATENT AND TRADEMARK OFFICE<br><br>INFORMATION DISCLOSURE<br>STATEMENT BY APPLICANT<br><br>(Use several sheets if necessary) | ATTY. DOCKET NO.<br>178-312 PCT/US | SERIAL NO.<br>10/519,534       |
|   | APPLICANT<br>Brown et al.          | CONFIRMATION NO.<br>Unassigned |
|   | FILING DATE<br>December 27, 2004   | GROUP<br>Unassigned            |

## U.S. PATENT PUBLICATIONS

| EXAMINER<br>INITIAL |  | DOCUMENT<br>NUMBER | DATE | NAME | CLASS | SUB<br>CLASS | FILING DATE<br>IF APPROPRIATE |
|---------------------|--|--------------------|------|------|-------|--------------|-------------------------------|
|                     |  |                    |      |      |       |              |                               |

## U.S. PATENT DOCUMENTS

| EXAMINER<br>INITIAL |  | DOCUMENT<br>NUMBER | DATE | NAME | CLASS | SUB<br>CLASS | FILING DATE<br>IF APPROPRIATE |
|---------------------|--|--------------------|------|------|-------|--------------|-------------------------------|
|                     |  |                    |      |      |       |              |                               |

## FOREIGN PATENT DOCUMENTS

| EXAMINER<br>INITIAL |  | DOCUMENT<br>NUMBER | DATE | COUNTRY | CLASS | SUB<br>CLASS | TRANSLATION |    |
|---------------------|--|--------------------|------|---------|-------|--------------|-------------|----|
|                     |  |                    |      |         |       |              | YES         | NO |
|                     |  |                    |      |         |       |              |             |    |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|  |  |  |   |
|--|--|--|---|
|  |  |  | Takeshita, Satoshi, et al. "Modulation of Oxidative Burst of Neutrophils by Doxycycline in Patients with Acute Myocardial Infarction," <i>Journal of Antimicrobial Chemotherapy</i> (2002) 49: 411-413. |
|  |  |  | Creemers, Esther E.J.M., et al., "Matrix Metalloproteinase Inhibition After Myocardial Infarction," <i>Circulation Research</i> (2001) 89: 201-210.   |
|  |  |  | Meier, Christoph R., et al., "Antibiotics and Risk of Subsequent First-time Acute Myocardial Infarction," <i>JAMA</i> (1999) 281(5): 427-431.   |

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication with applicant.

|   |                                    |                                |
|---|------------------------------------|--------------------------------|
| FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE<br>(Rev. 2-32) PATENT AND TRADEMARK OFFICE<br><br>INFORMATION DISCLOSURE<br>STATEMENT BY APPLICANT<br><br>(Use several sheets if necessary) | ATTY. DOCKET NO.<br>178-312 PCT/US | SERIAL NO.<br>10/519,534       |
|   | APPLICANT<br>Brown et al.          | CONFIRMATION NO.<br>Unassigned |
|   | FILING DATE<br>December 27, 2004   | GROUP<br>Unassigned            |

## U.S. PATENT PUBLICATIONS

| EXAMINER<br>INITIAL |  | DOCUMENT<br>NUMBER | DATE | NAME | CLASS | SUB<br>CLASS | FILING DATE<br>IF APPROPRIATE |
|---------------------|--|--------------------|------|------|-------|--------------|-------------------------------|
|                     |  |                    |      |      |       |              |                               |

## U.S. PATENT DOCUMENTS

| EXAMINER<br>INITIAL |  | DOCUMENT<br>NUMBER | DATE | NAME | CLASS | SUB<br>CLASS | FILING DATE<br>IF APPROPRIATE |
|---------------------|--|--------------------|------|------|-------|--------------|-------------------------------|
|                     |  |                    |      |      |       |              |                               |

## FOREIGN PATENT DOCUMENTS

| EXAMINER<br>INITIAL |  | DOCUMENT<br>NUMBER | DATE | COUNTRY | CLASS | SUB<br>CLASS | TRANSLATION |    |
|---------------------|--|--------------------|------|---------|-------|--------------|-------------|----|
|                     |  |                    |      |         |       |              | YES         | NO |
|                     |  |                    |      |         |       |              |             |    |

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|  |  |  |  |
|--|--|--|--|
|  |  |  | Ridker, Paul M., et al., "Long-Term Effects of Pravastatin on Plasma Concentration of C-reactive Protein," <i>Circulation</i> (1999) 100: 230-235.   |
|  |  |  | Brown, David L., et al., "Clinical and Biochemical Results of the Metalloproteinase Inhibition With Low-dose Doxycycline to Prevent Acute Coronary Syndromes (Midas) Pilot Trial," <i>American Heart Association</i> (2001). |
|  |  |  | Libby, Peter, "Atherosclerosis: The New View," <i>Scientific American</i> (2002) 48-55.  |

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication with applicant.

|   |                                    |                                |
|---|------------------------------------|--------------------------------|
| FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE<br>(Rev. 2-32) PATENT AND TRADEMARK OFFICE<br><br>INFORMATION DISCLOSURE<br>STATEMENT BY APPLICANT<br><br>(Use several sheets if necessary) | ATTY. DOCKET NO.<br>178-312 PCT/US | SERIAL NO.<br>10/519,534       |
|   | APPLICANT<br>Brown et al.          | CONFIRMATION NO.<br>Unassigned |
|   | FILING DATE<br>December 27, 2004   | GROUP<br>Unassigned            |

## U.S. PATENT PUBLICATIONS

| EXAMINER<br>INITIAL |  | DOCUMENT<br>NUMBER | DATE | NAME | CLASS | SUB<br>CLASS | FILING DATE<br>IF APPROPRIATE |
|---------------------|--|--------------------|------|------|-------|--------------|-------------------------------|
|                     |  |                    |      |      |       |              |                               |

## U.S. PATENT DOCUMENTS

| EXAMINER<br>INITIAL |  | DOCUMENT<br>NUMBER | DATE | NAME | CLASS | SUB<br>CLASS | FILING DATE<br>IF APPROPRIATE |
|---------------------|--|--------------------|------|------|-------|--------------|-------------------------------|
|                     |  |                    |      |      |       |              |                               |

## FOREIGN PATENT DOCUMENTS

[illegible]

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

|  |  |  |   |
|--|--|--|---|
|  |  |  | Kloppenburger, M., et al., "Minocycline in Active Rheumatoid Arthritis," <i>Annals of the New York Academy of Sciences</i> (1994) 732: 422-423. |
|--|--|--|---|

200178

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication with applicant.